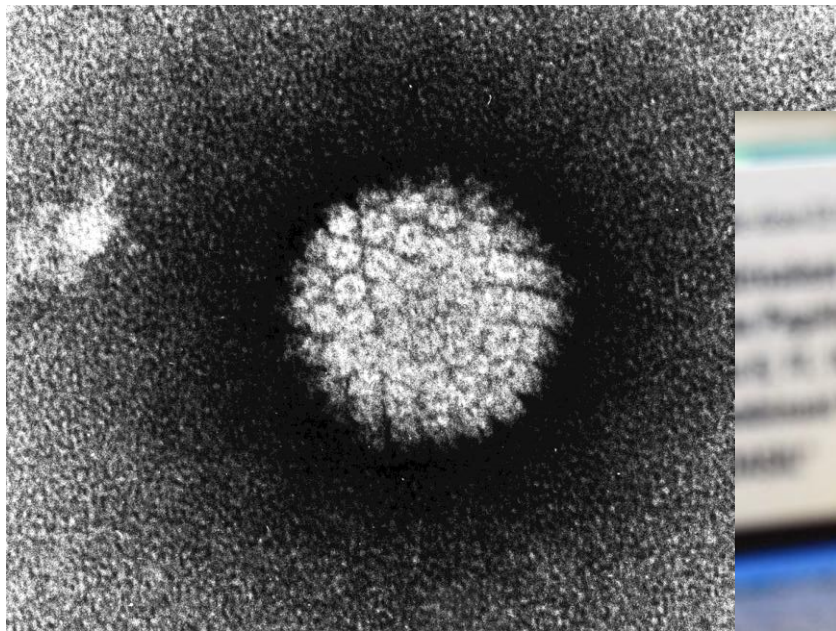


Public health impact of HPV vaccines: predictions of a dynamic model



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Conflict of Interest Declaration

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HPV and cervical cancer overview

- Papanicola (pap) testing was introduced in the 1960s, leading to a significant decline in cervical cancer incidence.
- But there has been little additional decline in Canada since the 1990s.
- HPV was identified as causative agent of cervical cancer in 1983 (Dürst *et al*, PNAS).
- Immunization programs of 9- to 13-year old females using the quadrivalent 6/11/16/18 HPV vaccine began in several Canadian provinces in 2007.

Questions

- The advent of HPV immunization has led to new questions.
 - Should cervical screening be modified?
 - Should we implement catch-up programs?
 - Booster shots? At what age? Vaccinate males?

- For primary prevention strategies, and integrated primary/secondary prevention strategies,
 - What is their effectiveness as measured by
 - Incidence of cervical cancer in various age groups over time?
 - Incidence of CIN1, CIN2/3 lesions in age groups over time?
 - What is their cost-effectiveness as measured by
 - Cost per life-year saved?

What is a transmission model?

- An infectious disease transmission model can be used to address many of these questions.
- Transmission models capture mechanisms of disease transmission.

$$I_{t+1} = T \times S_t \times I_t$$

T = transmission rate
 S_t = #susceptible, time t
 I_t = #infected, time t

- Examples: compartmental models, agent-based models, SIR models, network models, individual-based models...
- Can be used to project disease incidence, costs, other outcomes under various possible strategies.
- Need to be parameterized and validated against existing data.

Why use transmission models?

- Why use models?
 - Provides a virtual laboratory.
 - Makes assumptions explicit.
 - Provides a transparent framework that integrates disparate types of data.
- Why use transmission models?
 - Transmission models can capture herd immunity effects.
 - Herd immunity is often a significant source of protection for the unvaccinated.

Previous Work

- About 10-15 models (transmission or otherwise) have been published to date, analyzing HPV immunization programs.
- Brisson *et al* (2007) develop a model for a birth cohort of Canadian females vaccinated at age 12.
 - They estimate that you need to vaccinate
 - 324 (196-757) females to prevent 1 cervical cancer case
 - 729 (411-1921) to prevent 1 cervical cancer death
 - 16 (10-41) to prevent 1 year of lost life
 - Analysis assumes lifelong immunity, 95% efficacy against infection by types 16/18

Previous Work

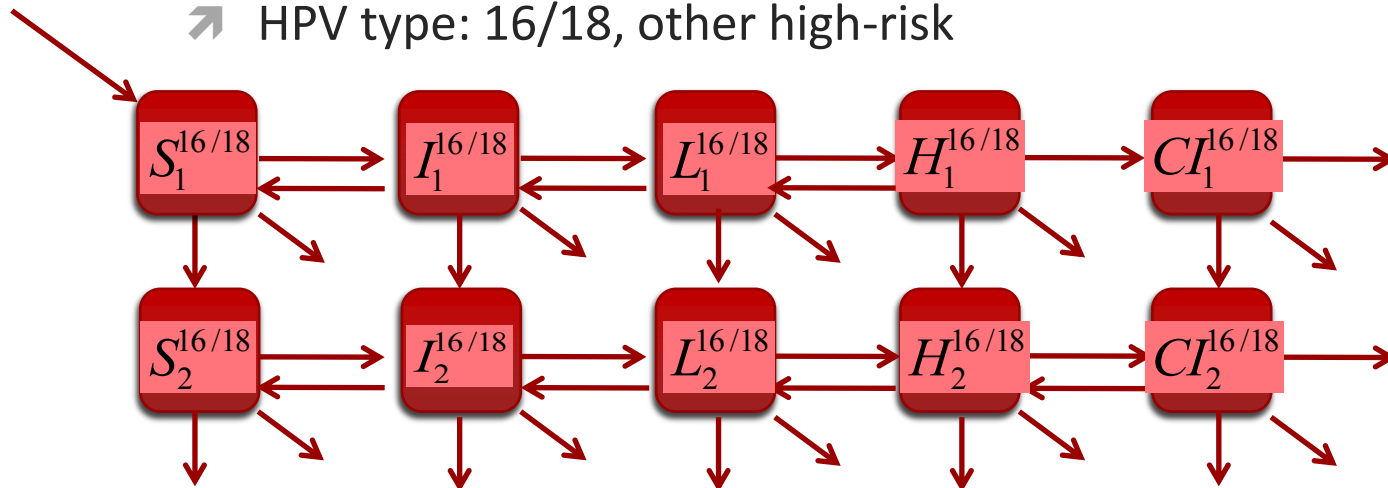
➤ Newall et al (2007) review three modelling studies.

	Sanders & Taira (2003)	Goldie et al (2004)	Taira et al (2004)
Model	Markov cohort	Markov cohort	Transmission
Efficacy	75% against 13 high-risk types	90% against types 16/18	90% against types 16/18
Coverage	70% of 12-year-old females	100% of 12-year-old females	70% of 12-year-old females
Durability	10 yrs (booster every 10 yrs)	Lifelong	10 yrs (booster every 10 yrs)
Cost-effectiveness	US \$22,755/QALY gained	US \$24,300/QALY gained	US \$14,583/QALY gained

➤ \$50,000/QALY is a commonly accepted threshold for CE.

Model Description

- Deterministic compartmental model
 - population stratified into compartments based upon
 - Age: 15-19, 20-24, 25-34, ..., 55-64, 65+
 - Gender: male or female (heterosexual only)
 - Infection status: susceptible, latently infected, CIN1, CIN2/3, CI-IV.
 - HPV type: 16/18, other high-risk



Model Description

- Sexual mixing is age assortative (Taira et al 2002)
- Bivalent vaccine efficacy
 - 95% against types 16/18
 - 12% against other high-risk types (Paavonen et al 2009).
- Waning immunity analyzed via sensitivity analysis
- Benign hysterectomy and deaths due to other causes included
- Simplified cervical screening/treatment module with age-dependent screening adherence rates
- Cervical cancer module tracks progression from CI-CIV

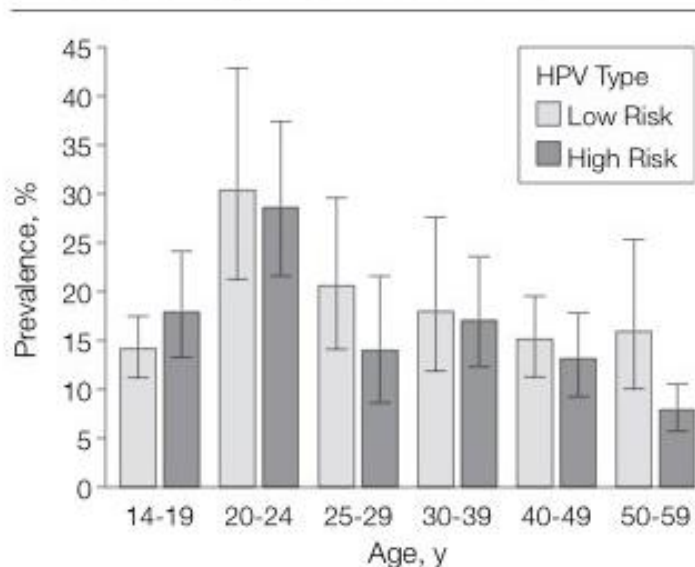
Model Description

- Outcomes projected by age and year:
 - Prevalence of infection
 - types 16/18
 - other high-risk types
 - Incidence of CIN1
 - Incidence of CIN2/3
 - Incidence of cervical cancer cases
 - Incidence of cervical cancer deaths
 - Costs for immunization, Pap testing and follow-up, CIN2/3 treatment, cancer treatment

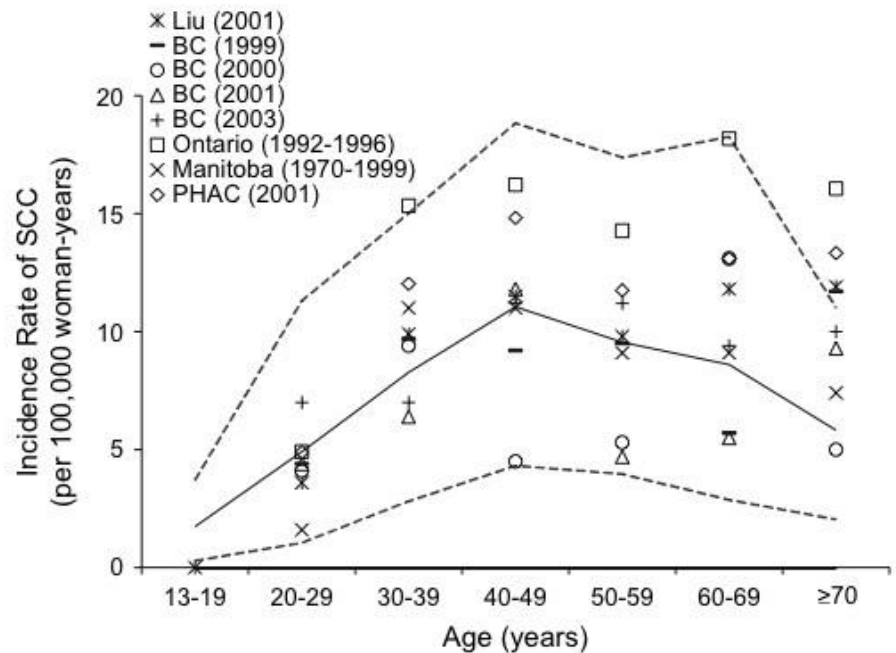
Model Parameterization

- Most parameter values taken directly from published literature, previously published models.
- Transmission rates and progression rates obtained by calibrating model to available data.

Figure 1. Prevalence of Low-Risk and High-Risk HPV Types Among Females Aged 14 to 59 Years, NHANES 2003-2004



Dunne et al, 2007

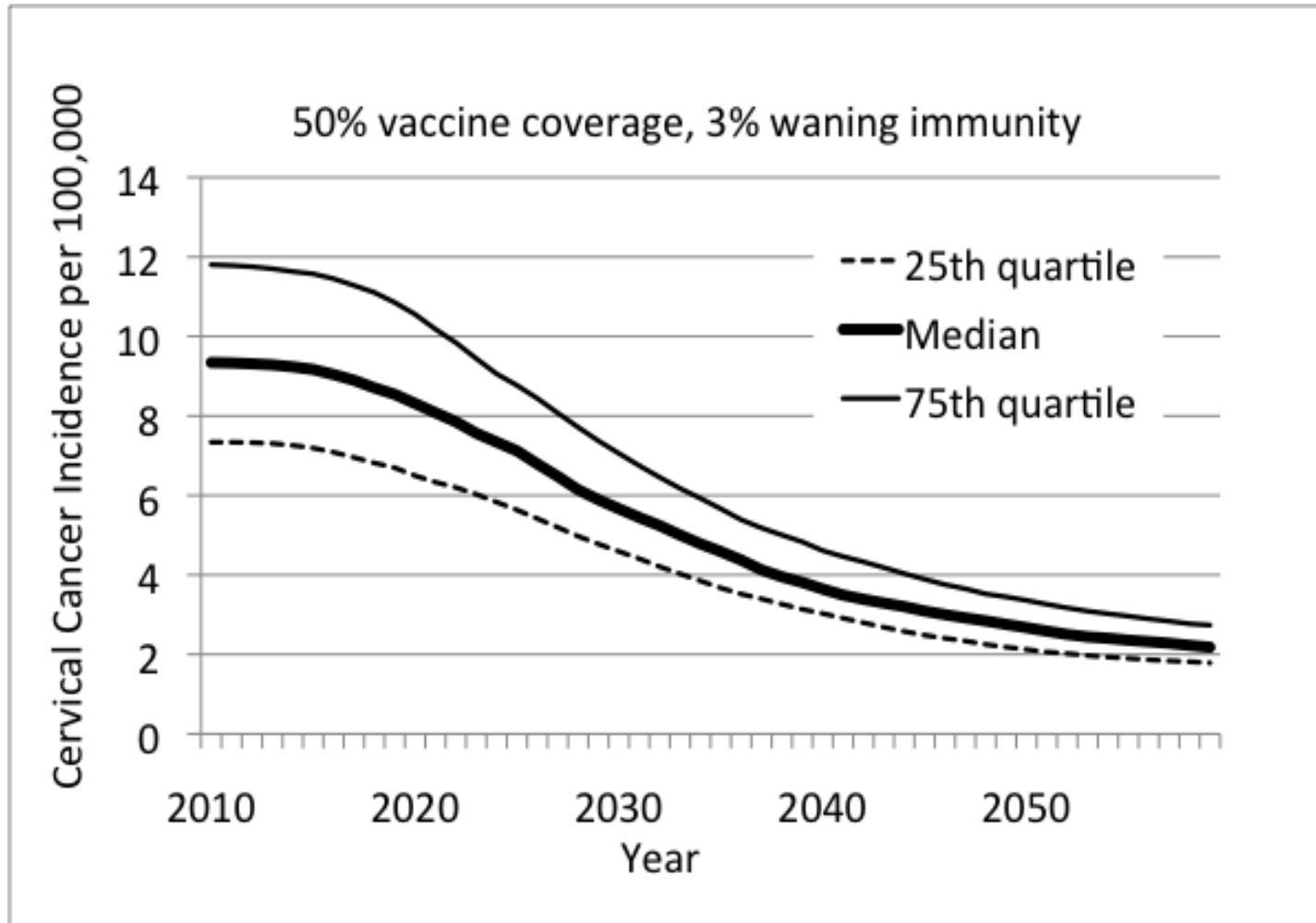


VanDeVelde et al, 2007

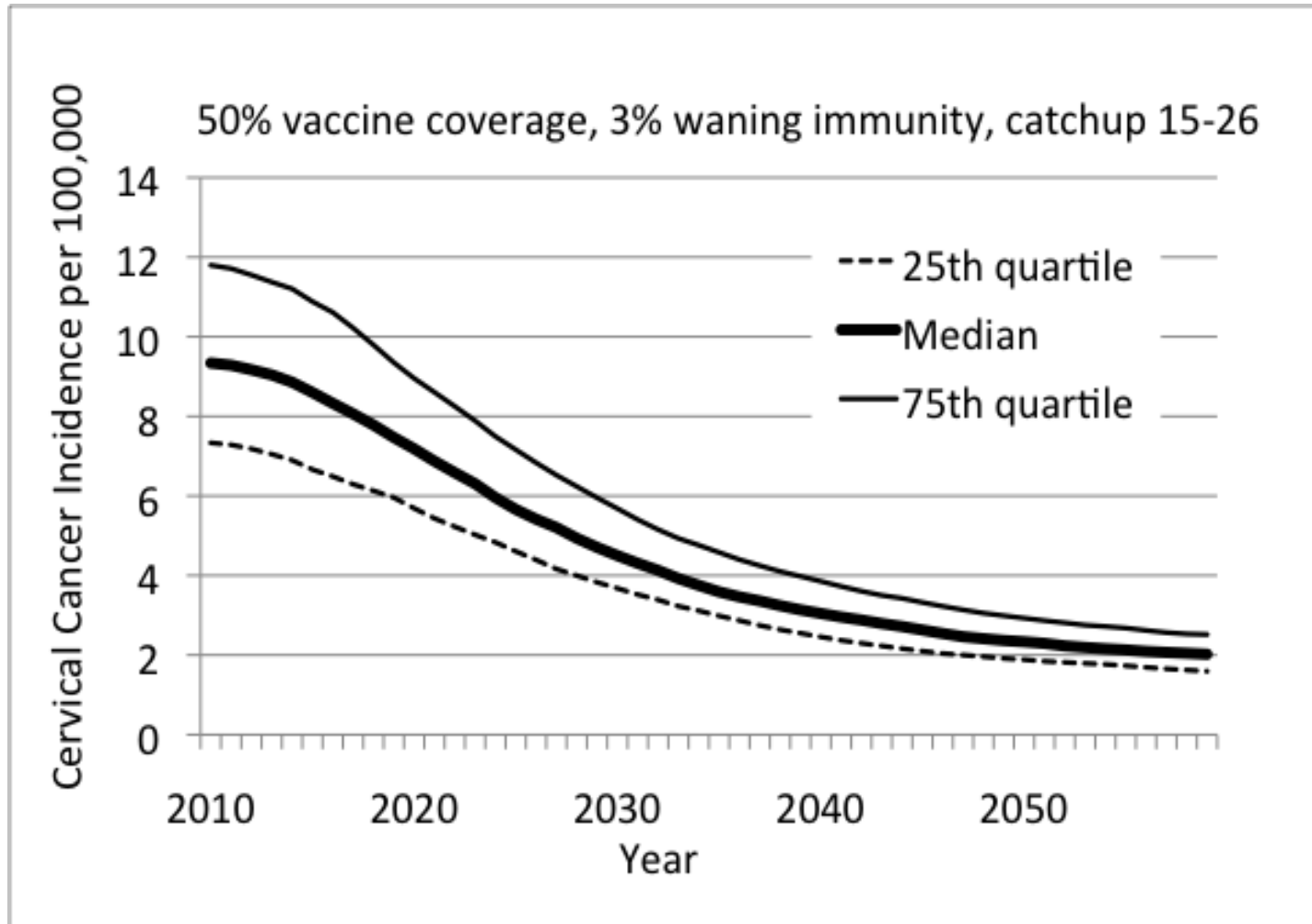
Scenarios

- Baseline scenario:
 - Vaccinating 12-year-old females only, starting in 2007, at 50% or 80% coverage
- Comparator scenarios:
 - Waning immunity: 3% per year
 - Single booster dose at age 25 (with 3% waning immunity)
 - Catch-up program in women aged 15-26
 - 50% reduction in screening rate

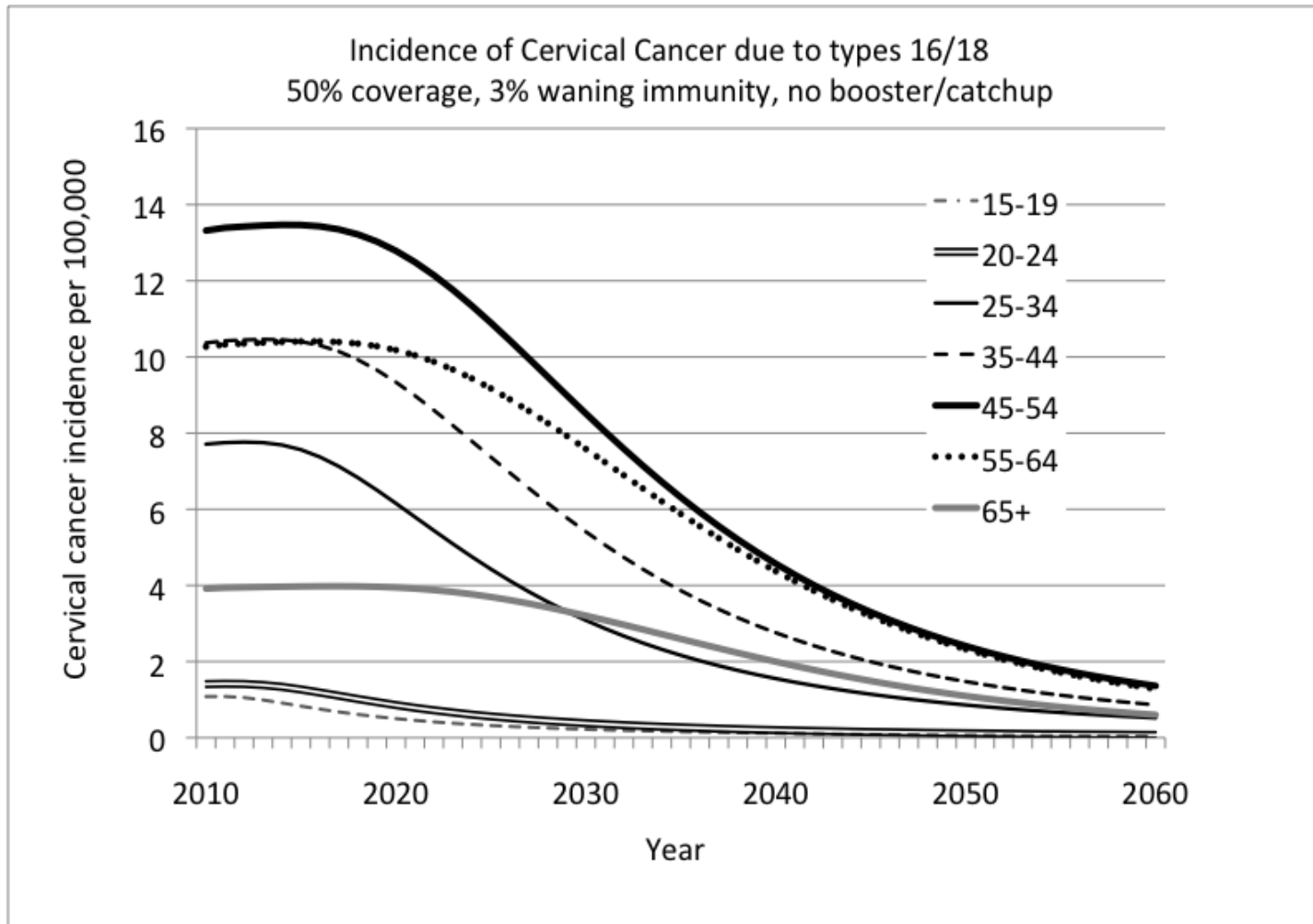
Preliminary results: time series



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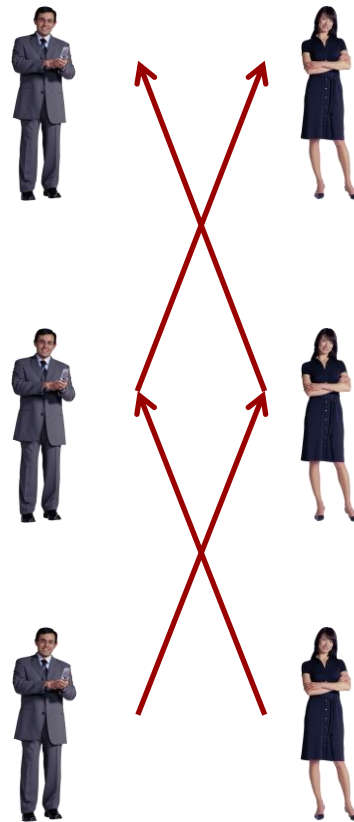


Preliminary results: timeseries

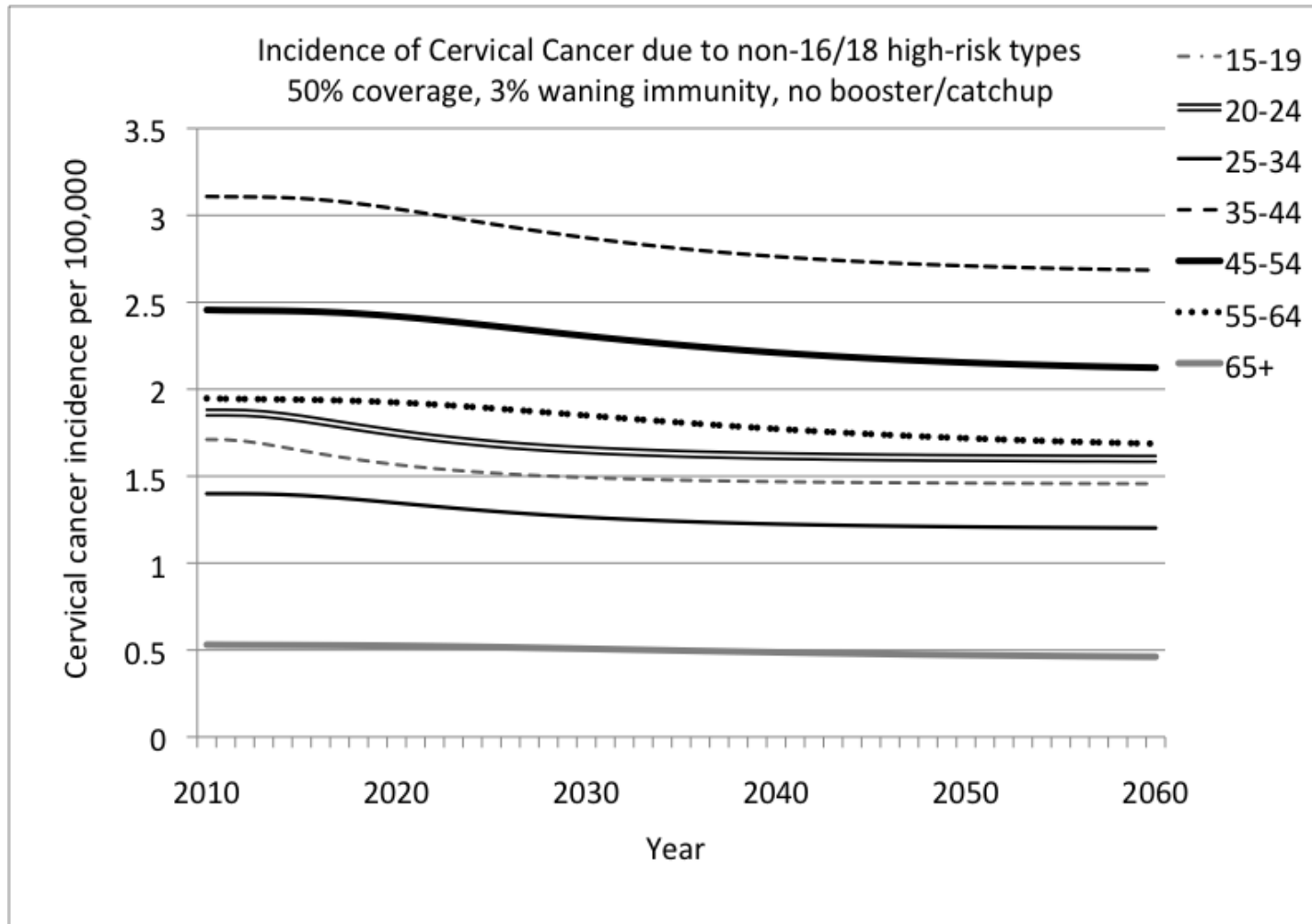


Herd immunity ladder

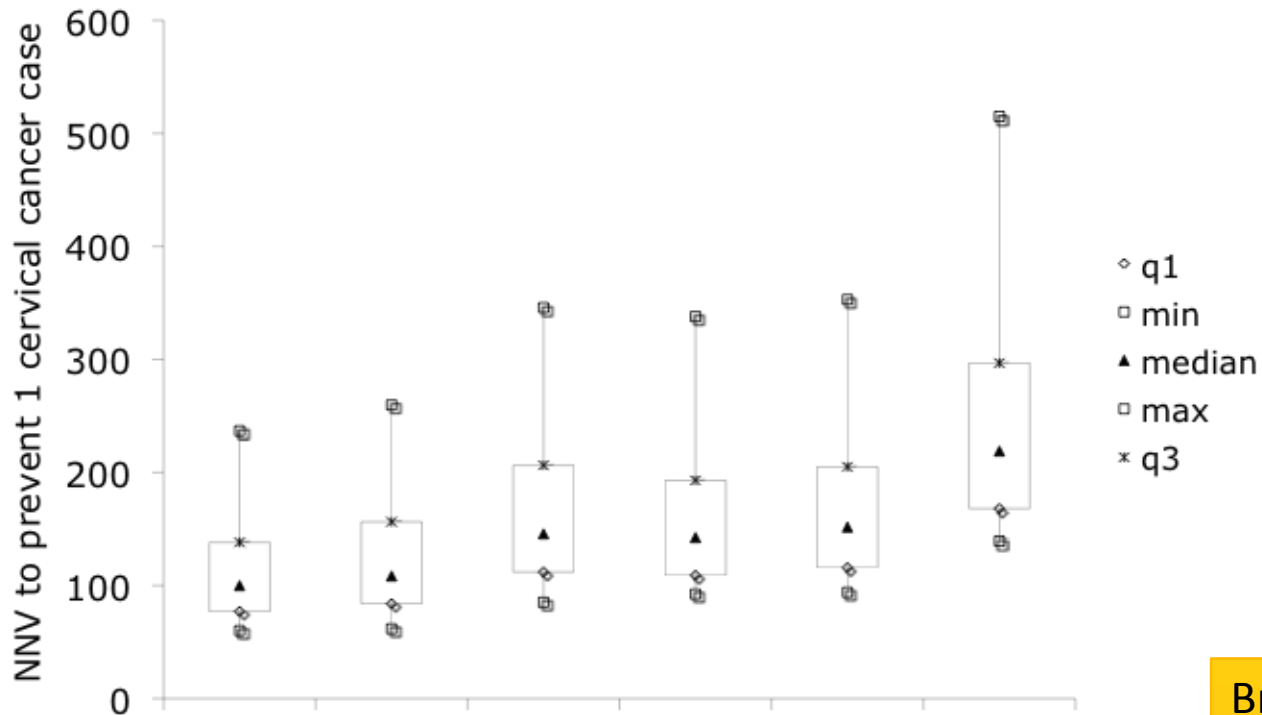
➔ Can herd immunity work its way up through the age distribution?



Preliminary results: time series



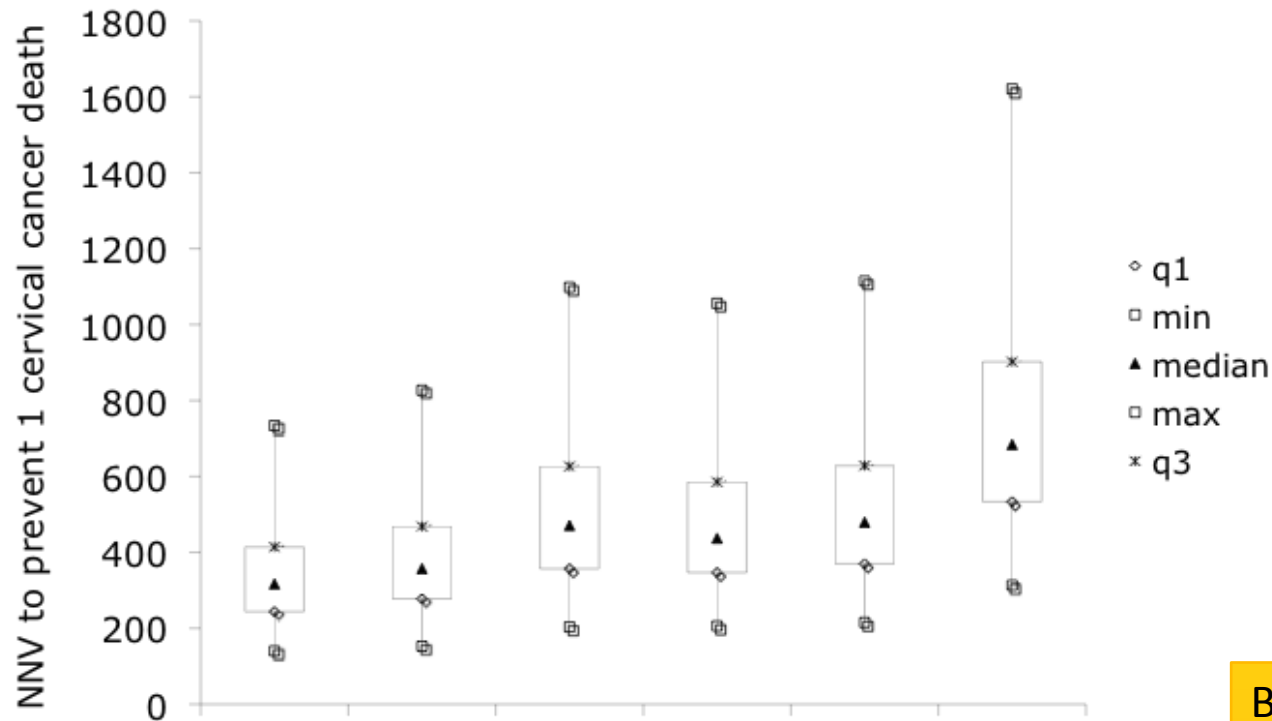
Preliminary results: number needed-to-vaccinate



Coverage	50%			80%		
Waning Immunity	None	3%	3%	None	3%	3%
Booster	No	No	Yes	No	No	Yes

**Brisson: 324
(196-757) to
prevent 1
cervical cancer
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Preliminary results: cost-effectiveness

➤ Cost-effectiveness and life-years saved (compared to no vaccine with normal screening rates).

Strategy	Cost per life-year saved	Life-years saved
Baseline	\$16,148 (\$4,788-\$27,509)	3,534 (1,575-5,493)
Waning immunity	\$17,513 (\$5,286-\$29,739)	3,378 (1,486-5,271)
Catch-up program	\$12,685 (\$4,103-\$21,220)	3,839 (1,886-5,787)
Reduced screening	Cost saving	3,139 (1,742-4,535)

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Conclusions

- Current HPV programs appear to be cost-effective, particularly if herd immunity is accounted for.
- Waning immunity doesn't change results very much.
- A catch-up program for females aged 15-26 saves the most life-years and is also more cost-effective than baseline.
- Lower screening is cost saving and still saves life-years relative to pre-vaccine era, but less effective than other strategies.
 - This suggests strategies such as rolling cost savings from lengthened screening intervals for most women into efforts to increase adherence in the remainder where adherence is insufficient.